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Research article

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Can intra-operative methylprednisolone application be effective for post-operative pain, nausea and vomiting in laparoscopic cholecystectomy operations?

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Ethics Committee Approval
This study was approved by the Uşak University Non-Interventional Clinical Research Ethics Committee, 135-08-11.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Post-operative nausea, vomiting (PONV), and pain are common symptoms after laparoscopic cholecystectomy (LC) that is performed under general anesthesia. These symptoms lead to prolongation of post-operative recovery and hospital stay. In this study, the efficacy of intra-operative methylprednisolone (MP) administration on post-operative pain and PONV was investigated in patients undergoing LC under general anesthesia.

Methods: This study was conducted at Uşak University Faculty of Medicine Hospital. Patients who underwent LC under general anesthesia between 01.11.2018 and 01.06.2019 were evaluated using the prospective cohort method. While intra-operative MP was administered to one group of patients who underwent LC (MP group), MP was not administered to the second group (non-MP). The pain was evaluated using the Visual Analog Scale (VAS) while PONV was evaluated with the Verbal Descriptive Scale (VDS in patients at post-operative hours 0, 1, 2, 6, 12, 18, and 24. On the first post-operative day, patient satisfaction was assessed.

Results: The study cohort consisted of 76 patients. The VAS was used to measure post-operative pain, and it was discovered that the MP group had significantly reduced VAS values at post-operative hours 0, 1, 2, 6, 12, 18, and 24 ($P < 0.001$). In the VDS evaluation, no difference between the two groups only at post-operative hour 12 ($P = 0.52$) was found, while the VDS value was found to be lower in the MP group than in the non-MP group at post-operative hours 0, 1, 2, 6, 18, and 24 ($P < 0.001$). The mean total analgesic use at post-operative hour 48 was 69.08 (26.91) mg in the MP group and 96.71 (42.38) mg in the non-MP group. The difference was statistically significant ($P < 0.001$).

Conclusion: PONV and discomfort incidence decreased after intra-operative MP administration. The decrease in these symptoms was positively reflected in post-operative patient satisfaction.

Keywords: Methylprednisolone, Postoperative pain, Postoperative nausea-vomiting

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Introduction

Nausea, pain, and vomiting are the main symptoms affecting post-operative patient comfort. These symptoms may lead to a prolongation of hospitalization and cause hospitalization again after discharge. Also, these symptoms are also included in the etiologies of complications, such as post-operative wound dehiscence, esophageal rupture, and pneumothorax [1]. While post-operative nausea and vomiting (PONV) occurs at a rate of around 30% in patients who do not receive prophylaxis, this rate may increase to 80% depending on a patient's individual predisposition [2, 3]. After gynecological and laparoscopic procedures, PONV is thought to occur more often. However, it is still controversial as to which operations trigger this situation more frequently [4]. If no prophylaxis is applied in laparoscopic cholecystectomy (LC) operations, the incidence of PONV is reported to be 53% to72% [5].

To achieve early mobilization, reduce the length of the hospital stay, and reduce complications, it is crucial to prevent post-operative pain. Opioids are frequently preferred for this purpose. Opioids, however, are also linked to PONV and other adverse effects. Therefore, minimizing the need for opioids and trying multimodal treatment methods are considered the most optimal strategy in post-operative pain management [6, 7].

It has been proposed that pre-operative glucocorticoids lead to a reduction in the incidence of PONV and may play a role in reducing post-operative pain [8, 9]. In this study, the efficacy of intra-operative methylprednisolone (MP) administration in relieving PONV and post-operative pain in patients undergoing LC was investigated.

Materials and methods

Patients who had elective LC surgery at Uşak University Medical Faculty Hospital were included in this study. The post-operative efficacy resulting from intra-operative MP administration was evaluated in the study. Participants in the study ranged in age from 18 to 70 and were American Society of Anesthesiologists (ASA) I-II patients. Those weighing < 50 kg or >120 kg, those with a body mass index (BMI) > 30, patients with ASA III-IV scores, those who had used any analgesic in the last 12 h, those with known gastritis and ulcer diagnosis or undergoing treatment, steroid users, those who were allergic to any of the study drugs to be used, those with aspartate transaminase (AST) >70 U/L, alanine aminotransferase (ALT) >110 U/L, and/or creatinine >2 mg/dl, and those with intellectual disability were excluded from the study. The study was conducted in accordance with the ethical standards specified in the Helsinki Declaration and was approved by the local ethics committee (Uşak University Non-Interventional Clinical Research Ethics Committee, 135-08-11). Written patient consent was obtained from the patient or the patient's spouse or legal guardian. Patient data were collected prospectively.

Selection of groups and collection of data

Intra-operative MP (2 mg/kg)was administered to one patient group (MP group), while intra-operative MP was not administered to the other group (non-MP group). Patients were assigned to the groups consecutively. Age, gender, BMI, duration of anesthesia, duration of surgery, and Apfel score (Table 1) of the patients were recorded.

Table 1: Apfel risk scoring

Risk factors	Score
Female gender	1
Not smoking	1
PONV story	1
Post-operative opioid use	1

PONV: Post-operative nausea and vomiting

Patients in both groups underwent surgery under general anesthesia. Each patient received 6 mg/kg thiopental, 0.6 mg/kg rocuronium bromide, and 0.5 mg/kg fentanyl in induction. For LC, 10 mm trocar entries were made 5 cm below the umbilicus and 5 cm below the xiphoid, and 5 mm trocar entry was from the right subcostal midclavicular and anterior axillary line. Intra-abdominal pressure (12 mmHg) was applied to the patients during LC. Anesthesia was maintained with 50% oxygen, 50% air mixture, and 2% sevoflurane. Inhalation anesthetics were stopped after placing the last skin suture. The patients were kept in the post-operative recovery unit for 1 h after which the patients with stable vital signs were transferred to the services. The patient's arrival in the post-operative recovery unit was considered as 0 min, and the patient's pain was evaluated and recorded with the VAS (Visual Analog Scale) at post-operative 0, 1, 2, 6, 12, 18, and 24 h. In the evaluation of the VAS, the patients were asked to score between 1 and 10 for their pain for which 0 indicated no pain and 10 reflected the worst possible pain. Also, whether the patients had nausea and vomiting at post-operative hours 0, 1, 2, 6, 12, 18, and 24 was evaluated with the Verbal Descriptive Scale (VDS) in this study. Severity of nausea and vomiting in the VDS assessment was classified into five groups: (1) None at all: 0; (2) Mild degree nausea: 1; (3) Moderate degree nausea: 2; (4) Frequently vomiting: 3; and (5) Severely vomiting: 4. No prophylactic antiemetic administration was given to the patients. The first post-operative analgesic requirement hours and total amount of analgesic consumption during the first post-operative 48 h were recorded. In case of post-analgesic requirements, 75 mg diclofenac sodium was administered intramuscularly to the patients. Patients were asked about their satisfaction on the first post-operative day. Scores were between 0 and 1 with 0: Not at all satisfied and 10: Very satisfied. Patients were asked to score accordingly.

Statistical analysis

According to how the groups were distributed, descriptive statistics for numerical variables were summarized as mean (standard deviation [SD]) or median with interquartile range (IQR). Mean parameter comparisons between groups with and without MP were obtained using with the independent-sample t test for normally distributed groups. For group comparisons in which no normal distribution was found, the Mann–Whitney U test was used. A 5% type 1 error level was considered statistically significant for all tests. Statistics Package for the Social Sciences 22.0 statistical package (IBM Corp.; Armonk, NY, USA) was used to conduct statistical analyses.

Results

G*power 3 software was used to determine the sample size. With a margin of error of 5% and a power of 0.80, 38 cases in each group were found to be sufficient to compare the

statistical significance of numerical variables between the MP and non-MP groups using the Mann–Whitney U test in the study. A total of 76 patients was included with 38 patients in each group.

A total of 76 patients in the study with 34 men and 42 women were assessed. The patients' average age was 44.6 (8.4) years. No differences between MP group and non-MP group were found in terms of age (P = 0.78), gender (P = 0.49), BMI (P = 0.33), duration of anesthesia (P = 0.22), surgery time (P = 0.80), and Apfel score (P = 0.37) as shown in Table 2. In the evaluation of the groups in terms of VAS, statistical significance in favor of the MP group (P < 0.001, Table 3) was observed. In terms of VDS, statistical significance was also found in favor of the MP group at other times, except at the 12th hour (P = 0.52, Table 3). The mean time for the need for the first post-operative analgesic administration was found to be 204.21 (37.02) min and 128.03 (11.71) min in the MP and non-MP groups, respectively (P < 0.001). Again, the amount of analgesic consumption in the first 48 h was significantly lower in the MP group (P < 0.001). The mean value of analgesic consumption was 69.08 (26.91) mg in MP group , whereas it was 96.71 (42.38) mg in the non-MP group. Patient satisfaction was evaluated on the first post-operative day. The median satisfaction score was found to be 8 (min: 5–max: 9) in patients belonging to the MP group and 6 (min: 4–max: 8) in the non-MP group (P < 0.001).

Table 2: Demographic distribution of groups

	MP group	Non-MP group	*P*-value
Gender (male/female)	16/22	18/20	0.49
Age (years) Mean (SD)	44.6 (8.4)	44.9 (7.1)	0.78
Anesthesia time (minutes) Mean (SD)	115.2 (8.8)	117.3 (9.2)	0.22
Surgery time (minutes) Mean (SD)	98.2 (9.4)	98.8 (9.5)	0.80
Apfel score median (min-max)	1 (0–3)	1(0–2)	0.37
BMI (kg/m^2) Mean (SD)	29.13 (3.9)	28.3 (4.7)	0.33

MP: Methyl prednisolone, BMI: Body mass index

Table 3: VAS and VDS evaluation of groups

	VAS 0	VAS 1	VAS 2	VAS 6	VAS 12	VAS 18	VAS 24
MP group (min–max)	5 (4–6)	5 (4–5)	4 (3–5)	4 (3–4)	3 (3–4)	2 (1–2)	1 (0–1)
Non-MP group (min–max)	6 (5–7)	6 (5–7)	6 (5–6)	5 (5–6)	5 (4–5)	4 (2–4)	3 (1-–3)
P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	VDS 0	VDS 1	VDS 2	VDS 6	VDS 12	VDS 18	VDS 24
MP group (min–max)	0 (0–1)	0 (0–1)	0 (0–2)	0 (0–2)	0 (0–3)	0 (0–2)	0 (0–2)
Non-MP group (min–max)	0 (0–1)	0 (0–1)	0 (0–3)	0 (0–4)	0 (0–4)	0 (0–4)	0 (0–4)
P-value	0.01	0.025	0.044	0.042	0.052	0.039	0.031

VAS: Visual Analog scale, VDS: Verbal Descriptive Scala

Discussion

Post-operative pain, nausea, and vomiting are frequent adverse effects of anesthesia. The incidence of PONV in all surgical procedures can be observed at a rate of 20 - 77%. Post-operative pain is closely associated with a prolonged recovery period [2, 10, 11]. Prevention of nausea, vomiting, and pain is very important for post-operative patient comfort. In this study, PONV and pain were observed less in patients who received intra-operative MP, and a higher level of patient satisfaction was achieved.

Wang et al. [12] reported that PONV was reduced after pre-operative administration of dexamethasone in LC patients. Also, Henzi et al. [13] obtained similar results in their study and found that 8 mg dexamethasone administered pre-operatively led to a reduction in PONV in LC patients. In a meta-analysis evaluation, it was stated that peri-operative single-dose glucocorticoid administration reduced the incidence of PONV in large abdominal operations [8]. Despite the results of this study, in a similar study conducted in laparoscopic appendectomy patients, it was suggested that pre-operative administration of8 mg dexamethasone did not produce a reduction in the incidence of PONV, and pre-operative dexamethasone administration was not recommended for the prevention of PONV [14]. In another study conducted in orthopedic surgery patients, 125 mg MP was administered pre-operatively, and it was found to lead to a reduction in PONV. However, inconsistent results were reported in several studies involving patients undergoing intra-abdominal surgery [15–17]. Nausea and vomiting are mediated by muscarinic M1, dopamine D2, histamine H1, 5-hydroxytryptamine (HT)-3, and neurokinin 1 neurotransmitter receptors [18]. It is stated that a single dose of glucocorticoids prevents nausea and vomiting by inhibiting the synthesis of prostaglandins and endogenous opioids [13]. In this study, 125 mg of MP was administered intra-operatively to patients with LC, and nausea and vomiting were evaluated using the VDS. PONV was found to be significantly less in the MP administered group compared to the non-administered patient group.

Pain is one of the most important causes of the prolonged recovery period after LC [11]. Opioids have been the mainstay in reducing post-operative pain. However, opioids may not be used in effective doses due to their side effects (constipation, sedation, neuroexcitation, delirium, and others). These side effects can lead to a worsening of the already impaired quality of life in patients. Therefore, a multimodal approach and new researches for postoperative pain control is being used. For this purpose, pre-operative use of glucocorticoids for post-operative pain control has become a current issue. Aabakke et al. [17] administered 125 mg MP pre-operatively to the patients who had undergone open hysterectomy and stated that it had no benefit in post-operative pain control. Consistent with this study, in a meta-analysis investigating the efficacy of glucocorticoids, nine studies conducted on major abdominal surgery reported that glucocorticoids did not lead to a reduction in post-operative pain [8]. On the other hand, Lunn et al. [15] reported that pre-operative administration of 125 mg MP reduced pain after orthopedic surgery. In another study evaluating post-operative pain in patients who underwent LC, it was revealed that 125 mg MP administered pre-operatively was effective in producing a reduction in post-operative pain [10]. Contradictory study results for pre-operatively administered glucocorticoids for postoperative pain control have been published. It has been suggested that the analgesic effect of glucocorticoids is related to edema reduction [8]. It has also been demonstrated that systemic corticosteroid administration leads to a reduction in tissue levels of bradykinin and reduction in pain by suppressing the release of neuropeptides from nerve endings [19, 20]. In parallel with this literature information, in this study, post-operative VAS values were significantly lower in the MP-administered group compared to the non-administered group. Also, it was determined that the total amount of post-operative analgesic consumption was less in the MP-administered group.

In a meta-analysis conducted by Waldron et al. [21], it was stated that pre-operative administration of 8 mg dexamethasone led to an increase in post-operative patient satisfaction. In another study addressing this issue, the post-operative comfort in patients who had received pre-operative MP was evaluated using a questionnaire. Parameters, such as sleep quality, PONV, unaided mobilization, and fatigue were questioned in the questionnaire, and it was revealed that preoperative MP administration did not increase patient satisfaction [14]. Preventing nausea and vomiting after surgery and reducing pain are important for patient comfort. In this study, a reduction in both PONV and post-operative pain was observed in MP administered patients. These results were also reflected in patient satisfaction for which post-operative patient satisfaction in the MP-administered group was significantly better than in the non-administered group.

Limitations

The study was conducted in a limited patient group, and our patients consisted of only LC patients. Therefore, our results do not cover all operations. In addition, this study was performed in a single center and was not compared with the placebo group.

Conclusion

In this study, it was demonstrated that intra-operative administration of 125 mg MP led to a decrease in PONV and post-operative pain. An increase in post-operative patient comfort associated with the reduction of these symptoms was detected.

References

1. Hill RP, Lubarsky DA, Phillips-Bute B, Fortney T, Creed MR, Glass PS, et al. Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. Anesthesiology. 2000 Apr;92(4):958-67.
2. Kaya Z, Kaya S, Ölmez G. The effect of granisetron dexamethasone combination on postoperative nausea and vomiting in gynecological operations Dicle Med J. 2010;37(2):109-14.
3. Kranke P, Eberhart LH, Toker H, Roewer N, Wulf H, Kiefer P. A prospective evaluation of the POVOC score for the prediction of postoperative vomiting in children. Anesth Analg. 2007 Dec;105(6):1592-7.
4. Apfel CC, Heidrich FM, Jukar-Rao S, Jalota L, Hornuss C, Whelan RP, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. Br J Anaesth. 2012 Nov;109(5):742-53.
5. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Ramosetron vs granisetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Can J Anaesth. 1999 Oct;46(10):991–3.
6. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. JAMA Intern Med. 2016 Sep; 176(9):1286-93.
7. Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia I: physiological pathways and pharmacological modalities. Can J Anaesth. 2001 Nov; 48(10):1000-10.
8. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. J Am Coll Surg. 2002 Nov;195(5):694–712.
9. .Rich WM, Abdulhayoglu G, DiSaia PJ. Methylprednisolone as an antiemetic during cancer chemotherapy – a pilot study. Gynecol Oncol. 1980 Apr;9(2):193–8.
10. Gautam S, Agarwal A, Das PK, Agarwal A, Kumar S, Khuba S. Evaluation of the efficacy of methylprednisolone, etoricoxib and a combination of the two substances to attenuate postoperative pain and PONV in patients undergoing laparoscopic cholecystectomy: a prospective, randomized, placebo-controlled trial. Korean J Pain. 2014 Jul;27(3):278–84.
11. Lau H, Brooks DC. Predictive factors for unanticipated admissions after ambulatory laparoscopic cholecystectomy. Arch Surg. 2001 Oct;136(10):1150-3.
12. Wang JJ, Ho ST, Liu YH, Lee SC, Liu YC, Liao YC, et al. Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy. Br J Anaesth. 1999 Nov;83(5):772-5.
13. Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg. 2000 Jan;90(1):186–94.
14. Kleif K, Hauge CI, Vilandt J, Gögenur I. Randomized Clinical Trial of Preoperative High-Dose Methylprednisolone on Postoperative Pain at Rest After Laparoscopic Appendectomy. Anesth Analg. 2018 May;26(5):1712-20.
15. Lunn TH, Kristensen BB, Andersen LØ, Husted H, Otte KS, Gaarn-Larsen L, et al. Effect of high-dose preoperative methylprednisolone on pain and recovery after total knee arthroplasty: a randomized, placebo-controlled trial. Br J Anaesth. 2011 Feb;106(2):230–8.
16. Lunn TH, Andersen LØ, Kristensen BB, Husted H, Gaarn-Larsen L, Bandholm T, et al. Effect of high-dose preoperative methylprednisolone on recovery after total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. Br J Anaesth. 2013 Jan;110(1):66–73.
17. Aabakke AJ, Holst LB, Jørgensen JC, Secher NJ. The effect of a preoperative single-dose methylprednisolone on postoperative pain after abdominal hysterectomy: a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2014 Sep;180:83–8.
18. Bashashati M, McCallum RW. Neurochemical mechanisms and pharmacologic strategies in managing nausea and vomiting related to cyclic vomiting syndrome and other gastrointestinal disorders. Eur J Pharmacol. 2014 Jan;722:79-94.
19. Hargreaves KM, Costello A. Glucocorticoids suppress levels of immunoreactive bradykinin in inflamed tissue as evaluated by microdialysis probes. Clin Pharmacol Ther. 1990 Aug;48(2):168–78.
20. Hong D, Byers MR, Oswald RJ. Dexamethasone treatment reduces sensory neuropeptides and nerve sprouting reactions in injured teeth. Pain 1993 Nov;55(2):171–81.
21. Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. Br J Anaesth. 2013 Feb;110(2):191–200.

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